REMARKS

Interview request

Applicants respectfully request a telephonic interview after the Examiner has reviewed the instant response and amendment. Applicants request the Examiner call Applicants' representative at 858 720 5133.

Status of the Claims

Pending claims

Claims 93 to 137 are pending.

Claims canceled and added in the instant amendment

In the present response, claims 138 to 152 are added, and, claims 96 to 98 and 133 to 137 are canceled, without prejudice. Accordingly, after entry of the instant amendment, claims 93 to 95, 99 to 132 and 138 to 152 will be pending and under examination.

Outstanding Rejections

Claims 93 to 103, 105 to 128, 131 and 132 are rejected under 35 U.S.C. §112, second paragraph. The rejection of claims 105 to 115 is maintained, and claims 118, 119 as amended and new claims 129 to 132 are rejected under 35 U.S.C. §112, first paragraph. Applicants respectfully traverse all outstanding objections to the specification and rejection of the claims.

Claim 104 Allowable

Applicants thank the Examiner for finding claim 104 allowable.

Support for the Claim Amendments

The specification sets forth an extensive description of the invention in the new and amended claims. Support for claims directed to methods for making a polypeptide using a nucleic acid of the invention can be found, *inter alia*, on page 21, line 25 to page 25.

Information Disclosure Statement

Applicants thank the Examiner for expressly considering (and initialing) the submitted Information Disclosure Statements (IDSs) and Forms PTO-1449.

Issues under 35 U.S.C. §112, second paragraph

As discussed in paragraphs 4 to 13, pages 3 to 5, of the instant office action, claims 93 to 103, 105 to 128, 131 and 132 stand rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. The rejection of claims 105 to 115 is maintained, and claims 118, 119 as amended and new claims 129 to 132 stand rejected under the written description requirement of 35 U.S.C. §112, first paragraph. The instant amendment addresses these issues.

Issues under 35 U.S.C. §112, first paragraph

Written Description

The rejection of claims 105 to 115 is maintained, and claims 118, 119 as amended and new claims 129 to 132 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors at the time the application was filed had possession of the claimed invention.

Applicants thank the Patent Office for acknowledging that (1) the instant claims now recite a specific function for the claimed polypeptides, (2) a test for activity is provided in the application, (3) assessing percent homology is well known in the art; and, (4) a skilled artisan is well-versed in protocols used for biological research (please see paragraph 14, page 5, of the office action mailed March 26, 2003). The Patent Office also notes that a genus of polypeptides can be achieved by a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus.

Applicants respectfully maintain that the claimed invention is sufficiently described in the specification so that one of ordinary skill in the art would be able to ascertain the scope of the claims with reasonable clarity and recognize that Applicants' were in possession of the claimed invention at the time of filing.

The Patent Office remains concerned that not claims 105 to 115, 118, 119, and 129 to 132, do not recite a functional limitation. Applicants believe the instant amendment addresses the Patent Office's concerns. All of the pending claims directed to polypeptides

should now unambiguously recite a functional limitation (or, as with the isolated or recombinant polypeptide having a sequence as set forth in SEQ ID NO:4, the polypeptide unambiguously has alpha galactosidase activity). Polypeptides not having alpha galactosidase activity are outside of the scope of the claimed invention.

Additionally, Applicants believe the instant amendment addresses the Patent Office's concerns regarding the scope of the genus of nucleic acids or polypeptides used in the claimed methods of the invention. The claims now read on a genus of polypeptides having 70% sequence identity to the exemplary sequence, or, being encoded by a nucleic acid having 70% sequence identity to the exemplary sequence.

The Patent Office remains concerned, inter alia, that there is no disclosure as to which structural features in an exemplary sequence, e.g., a fragment of an exemplary enzyme, or a polypeptide having a percent sequence identity to the exemplary enzyme, are responsible for enzymatic activity (please note paragraph 18 of the instant office action).

Applicants again respectfully refer to the USPTO guidelines concerning compliance with the written description requirement of U.S.C. §112, first paragraph. In example 14 of the guidelines (a copy of which is attached as Exhibit A), a claim reciting variants claimed by sequence identity to a sequence is sought (specifically, "A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A → B). In the example, the specification is described as providing SEQ ID NO:3 and a function for the protein. The specification contemplates, but does not exemplify variants of SEQ ID NO:3 that can have substitutions, deletions, insertions and additions. Procedures for making proteins with substitutions, deletions, insertions, and additions are routine in the art and an assay is described which will identify other proteins having the claimed catalytic activity. The analysis of example 14 states that procedures for making variants (which have 95% sequence identity) are conventional in the art. The Guidelines conclusion states that the disclosure meets the requirements of 35 U.S.C. §112, first paragraph, as providing adequate written description for the claimed invention.

The USPTO guidelines recognize that the written description requirement is met for a genus of polypeptides described by structure, a physico-chemical property (e.g., a % sequence identity, stringent hybridization) and a defined function. Procedures for making

enzyme variants were conventional in the art at the time of this invention. Accordingly, the claimed genus of polypeptides of this invention also meets the written description requirements of section 112.

Particularly addressing the Patent Office's concerns, Example 14 of the guidelines does not describe which structural features of the exemplary sequence are responsible for enzymatic activity. In Example 14, there is no disclosure as to which structural features or elements in the Example's exemplary polypeptide have the catalytic activity and can be modified such that a polypeptide having a percent sequence identity to the exemplary polypeptide would also have the same activity. Nevertheless, the USPTO guidelines state that Example 14 meets the requirements of 35 U.S.C. §112, first paragraph, as providing adequate written description for the claimed invention.

Analogous to the USPTO guidelines, the claimed polypeptides are described by structure (the exemplary nucleic acid or polypeptide sequences), a physico-chemical property (percent sequence identity) and function (alpha galactosidase activity). All polypeptides of the claimed genus must encode a polypeptide having alpha galactosidase activity and having at least about 70% sequence identity to SEQ ID NO:4, or, are encoded by a nucleic acid having at least about 70% sequence identity to SEQ ID NO:3, or, have conservative amino acid substitutions of the exemplary sequence and alpha galactosidase activity. Procedures for making enzyme variants or enzymatically active fragments were conventional in the art at the time of this invention.

Accordingly, Applicants respectfully submit that the pending claims meet the written description requirements under 35 U.S.C. §112, first paragraph. In light of the above remarks, Applicants respectfully submit that claimed invention is sufficiently described in the specification to overcome the rejection based upon 35 U.S.C. §112, first paragraph.

Enablement

The rejection of claims 93 to 102 and 105 to 119 is maintained, and new claims 120 to 127 and 129 to 132 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention.

The Patent Office states that the specification is enabling for the polypeptide of SEQ ID NO:4 and a composition comprising the polypeptide of SEQ ID NO:4

The Patent Office remains concerned that some of the pending claims directed to a polypeptide of the invention do not recite a functional limitation. Applicants believe the instant amendment addresses the Patent Office's concerns. All of the pending claims directed to polypeptides should now unambiguously recite a functional limitation (or, as with the isolated or recombinant polypeptide having a sequence as set forth in SEQ ID NO:4, the polypeptide unambiguously has alpha galactosidase activity). Polypeptides not having alpha galactosidase activity are outside of the scope of the claimed invention.

Additionally, Applicants believe the instant amendment addresses the Patent Office's concerns regarding the scope of the genus of nucleic acids or polypeptides used in the claimed methods of the invention. The claims now read on a genus of polypeptides having 70% sequence identity to the exemplary sequence, or, being encoded by a nucleic acid having 70% sequence identity to the exemplary sequence.

The Patent Office also maintains its allegation that because, inter alia, there is no guidance or knowledge as to which are the critical structural elements or features in the polypeptide of SEQ ID NO:4 that correlate with alpha galactosidase activity, it would not be routine to randomly create an infinite number of variants and test them for activity.

Applicants respectfully maintain that the specification enabled the skilled artisan at the time of the invention to identify, and make and use, a genus of alpha galactosidases to practice the claimed invention. As declared by Dr. Jay Short (please also note previously submitted Rule 132 declaration), the state of the art at the time of the invention and the level of skill of the person of ordinary skill in the art, e.g., screening enzymes, and nucleic acids encoding enzymes, for alpha galactosidase activity, was very high. In particular, Dr. Short, an expert in the field of molecular biology and enzyme development at the time of the invention, declared that it would not have required any knowledge or guidance as to which are the specific structural elements, e.g., amino acid residues, that correlate with alpha galactosidase activity to create variants of the exemplary nucleic acid and test them for the expression of polypeptides having alpha galactosidase activity. Dr. Short also declares that it would not have required any knowledge or guidance as to which are the specific structural elements, e.g., amino acid residues,

that correlate with alpha galactosidase activity to create variants or fragments of the exemplary polypeptides and test them for the expression of polypeptides having alpha galactosidase activity.

To clarify and further address this issue, Dr. Short further declares that it was not necessary for the skilled artisan to understand which specific regions of alpha galactosidase sequence or structure needed to be modified without affecting function or activity to routinely generate the genus of alpha galactosidases of this invention. Dr. Short declares that methods for sequence modifications were sufficiently comprehensive, routine and predictable at the time of the invention to predictably generate alpha galactosidase-encoding sequences or protein sequences without need of knowing which specific regions of alpha galactosidase sequence or structure affected alpha galactosidase function or activity. Dr. Short declares that methods known at the time of the invention for modifying nucleic acid or protein sequences in combination with high through-put enzyme activity screening known at the time of the invention, made methods that require previous knowledge of protein structure, including secondary or tertiary structure, active site sequences, and the like obsolete and unnecessary. Dr. Short declares that using methods known in the art at the time of the invention it would not have been necessary to understand which specific regions of alpha galactosidase structure needed to be modified to generate a genus of nucleic acids or polypeptides for practicing the invention without undue experimentation. Dr. Short declares that using methods known in the art at the time of the invention it would not have been necessary to understand what may be critical structural features or elements of an alpha galactosidase to generate the genus of polypeptides of the invention without undue experimentation.

Enablement is not precluded by the necessity to screen large numbers of alternative compounds (e.g., nucleic acids or polypeptides), as long as that screening is "routine," i.e., not "undue." As declared by Dr. Short, it would have taken only routine protocols to making variants of the exemplary nucleic acids and screen them to identify those that encode polypeptides with alpha galactosidase activity. Thus, the specification enabled the skilled artisan at the time of the invention to make and use a broad genus of alpha galactosidase. Accordingly, it would not have taken undue experimentation to make and use the claimed invention, including identification, making and using the claimed genus of alpha galactosidases.

Applicants respectfully submit that the pending claims meet the enablement requirement under 35 U.S.C. §112, first paragraph. In light of the above remarks, Applicants respectfully submit that the specification sufficiently described how to make and use the claimed methods to satisfy the requirements of 35 U.S.C. §112, first paragraph.

CONCLUSION

In view of the foregoing amendment and remarks, it is believed that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first and second paragraphs. Applicants believe all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants believe that no additional fees are necessitated by the present response and amendment. However, in the event any such fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 03-1952. Please credit any overpayment to this account.

As noted above, Applicants have requested a telephone conference with the undersigned representative to expedite prosecution of this application. After the Examiner has reviewed the instant response and amendment, please telephone the undersigned at 858 720 5133.

Respectfully submitted,

Date: May 19, 2004

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